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# INFORMATION DISCLOSURE STATEMENT

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| Attorney Docket | CHOR-003 |
| First Named Inventor | SHACKLETON, CEDRIC |
| Application Number | 10/077,577 |
| Confirmation No. | 1578 |
| Filing Date | February 15, 2002 |
| Group Art Unit | 1625 |
| Examiner Name | Unassigned |
| Title: "DIAGNOSIS OF SMITH-LEMLI-OPTIZ SYNDROME" | |

Sir:

This is an Information Disclosure Statement submitted for the Examiner's consideration. A Form PTO-SB/08A listing the references and copies of the cited references accompany this paper. Applicants would appreciate the Examiner's initialing and returning the form to indicate that the references have been reviewed and made of record.

This Information Disclosure Statement is not intended as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one of the above references constitutes prior art to the present application within the meaning of 35 U.S.C.§102.

As applicants have not yet received a first Action on the merits, no fee is believed to be required for filing this Disclosure Statement. If, however, the PTO finds that for some reason a fee is due, our Deposit Account No. 50-0815, Order No. CHOR-003 may be charged thereon.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 14, 2002

By: _____
Carol L. Francis
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Sheet 1 of 4

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| Application Number | 10/077,577 |
| Filing Date | February15, 2002 |
| First Named Inventor | Cedric Shackleton |
| Group Art Unit | Unassigned |
| Examiner Name | Unassigned |
| Attorney Docket Number | CHOR-003 |

## U.S. PATENT DOCUMENTS

| Examiner Initials' | Cite No.[1] | U.S. Patent Documents Number | Kind Code[2] (if known) | Name of Patentee or Applicant of Cited Documents | Date of Publication of Cited Document MM-DD-YYYY | Pages, columns, lines, Where Relevant Passages or Relevant Figures Appear |
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| | | | WO 01/92893 | | Schroepfer, et al. | 12-06-01 | | |

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|---|---|---|---|
| | | ABUELO, et al. "Prenatal detection of the cholesterol biosynthetic defect in the Smith-Lemli-Opitz syndrome by the analysis of amniotic fluid sterols", *Am J Med Genet*, (1995) Vol. 56: 281-285. | |
| | | ANDERSSON, et al. "Adrenal insufficiency in Smith-Lemli-Opitz Syndrome", *Am. J. Med Genet*, (1999) Vol. 82 (5): 382-384. | |
| | | BRADLEY, et al. "Levels of unconjugated estriol and other maternal serum markers in pregnancies with Smith-Lemli-Opitz (RSH) syndrome fetuses", *Am J Med Genet*, (1999) Vol. 82: 355-358. | |
| | | CLAYTON. "Disorders of cholesterol biosynthesis", *Arch. Dis. Child*, (1998) Vol. 78: 185-189. | |
| | | DALLAIRE, et al. "Prenatal diagnosis of Smith-Lemli-Opitz syndrome is possible by measurement of 7-dehydrocholesterol in amniotic fluid", *Prenat. Diagn.*, (1995) Vol. 15: 855-858. | |
| | | DONNAI, et al. "The lethal multiple congenital anomaly syndrome of polydactyly, sex reversal, renal hypoplasia, and unilobular lungs", *J. Med. Genet.* (1986) Vol. 23: 64-71. | |

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| | | FITZKY, et al. "Mutations in the delta-7-sterol reductase gene in patients with the Smith-Lemli-Opitz syndrome", *Proc. Natl. Acad. Sci. USA*, (1998) Vol. 95: 8181-8186. | |
| | | GLASS, et al. "Steroid sulphatase deficiency is the major cause of extremely low oestriol production at mid-pregnancy: A urinary steroid assay for the discrimination of steroid sulphatase deficiency from other causes", *Prenat. Diagn.*, (1998) Vol. 18: 789-800. | |
| | | IRONS, et al. "Defective cholesterol biosynthesis in Smith-Lemli-Opitz syndrome", *Lancet*, (1993) Vol. 341: 1414. | |
| | | IRONS, et al. "Prenatal diagnosis of Smith-Lemli-Opitz syndrome", *Prenat. Diagn.*, (1998) Vol. 18: 369-372. | |
| | | KELLEY. "Inborn errors of cholesterol biosynthesis", *Adv. Pediat.*, (2000) Vol. 47: 1-53. | |
| | | KRATZ, et al. "Prenatal diagnosis of the RSH/ Smith-Lemli-Opitz syndrome", Am. J. Med. Genet. Vol. 82: 376-381 (1999). | |
| | | MCGAUGHRAN, et al. "Prenatal diagnosis of Smith-Lemli-Opitz syndrome", Am. *J. Med. Genet.*, (1995) Vol. 56: 269-271. | |
| | | MCKEEVER, et al. "Smith-Lemli-Opitz syndrome II: A disorder of the fetal adrenals?", *J. Med. Genet.*, (1990) Vol. 27: 465-466. | |
| | | MILLS, et al. "First trimester prenatal diagnosis of Smith-Lemli-Opitz syndrome (7-dehydrochloesterol) reductase deficiency", *Pediatr. Res.*, (1996) Vol. 39: 816-819. | |
| | | MOEBIUS, et al. "Molecular cloning and expression of the human delta 7-sterol reductase", *Proc. Natl. Acad. Sci. USA*, (1998) Vol. 95: 1899-1902. | |
| | | PALOMAKI, et al. "Maternal serum screening for Down syndrome in the United States: A 1995 survey", *Am. J. Med. Genet.*, (1997) Vol. 176: 1046-1051. | |

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| Group Art Unit | Unassigned |
| Examiner Name | Unassigned |
| Attorney Docket Number | CHOR-003 |

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| | | ROSSITER, et al. "Smith-Lemli-Opitz Syndrome: Prenatal diagnosis by quantification of cholesterol precursors in amniotic fluid", *American Journal of Medical Genetics*, (1995) Vol. 56: 272-275. | |
| | | SHACKLETON. "Mass spectrometry in the diagnosis of steroid-related disorders and in hypertension research", *J. Steroid Biochem. Molec. Biol.*, (1993) Vol. 45: 127-140. | |
| | | SHACKLETON, et al. "Equine type estrogens produced by a pregnant woman carrying a Smith-Lemli-Opitz syndrome fetus", *J. Clin. Endrocrinol. Metab.*, (1999) Vol. 84: 1157-1159. | |
| | | SHACKLETON, et al. "Midgestational maternal urine steroid markers of fetal Smith-Lemli-Opitz syndrome (7-dehydrocholesterol 7-reductase deficiency)", *Steroids*, (1999) Vol. 64: 446-452. | |
| | | SHACKLETON, et al. "Neonatal urinary steroids in Smith-Lemli-Opitz Syndrome associated with 7-dehydrocholesterol reductase deficiency", *Steroids*, (1999) Vol. 64:481-490. | |
| | | SHACKLETON, et al. "Dehydro-oestriol and dehydropregnanetriol are candidate analytes for prenatal diagnosis of Smith-Lemli-Opitz syndrome", *Prenat. Diagn.*, (2001) Vol. 21: 207-212. | |
| | | SHARP, et al. "First-trimester diagnosis of Smith-Lemli-Opitz syndrome", *Prenat. Diagn.*, (1997) Vol. 17(4): 355-361. | |
| | | SMITH, et al. "A newly recognized syndrome of congenital nomalies", *J. Pediat.*, (1964) Vol. 64: 210-221. | |
| | | STEINER, et al. "Smith-Lemli-Opitz syndrome",*eMedicine J.*, (April 4, 2001) Vol. 2(4). | |
| | | STEINER, et al. "Smith-Lemli-Opitz syndrome", *eMedicine J.*, (February 5, 2002) Vol. 3(2). | |
| | | TINT, et al. "Defective cholesterol biosynthesis associated with the Smith-Lemli-Opitz syndrome", *N. Engl. J. Med.*, (1994) Vol. 330: 107-113. | |

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| | | TINT, et al. "Fetal Smith-Lemli-Opitz syndrome can be detected accurately and reliably by measuring amniotic fluid dehydrocholesterols", *Prenat. Diagn.*, (1998) Vol. 18: 651-658. | |
| | | Waterham, et al. "Smith-Lemli-Opitz Syndrome is Cuased by Mutations in the 7-Dehydrocholesterol Reducatse Gene", *Am. J. Hum. Genet.*, (1998) Vol. 63: 329-338. | |

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